The Office Action asserts that the Declaration under 37 C.F.R. §1.132 of Dr. Caldwell is insufficient to overcome the rejections because the results submitted are purportedly not commensurate in scope with the claims. In particular, the Office Action states that the claims include cis and trans and R and S isomers, whereas the data in the Declaration relate to trans compounds, and more particularly, to S isomers of trans compounds. Applicants respectfully disagree.

The claims all relate to cis and trans, R and S isomers of one particular compound, and therefore, read on just four compounds, (2S)-(4E)-N-methyl-5-(5-isopropoxy-3-pyridyl)-4-penten-2-amine, (2S)-(4Z)-N-methyl-5-(5-isopropoxy-3-pyridyl)-4-penten-2-amine, (2R)-(4E)-N-methyl-5-(5-isopropoxy-3-pyridyl)-4-penten-2-amine, and (2R)-(4Z)-N-methyl-5-(5-isopropoxy-3-pyridyl)-4-penten-2-amine. The binding properties and bioavailability of two of these compounds ((2S)-(4E)-N-methyl-5-(5-isopropoxy-3-pyridyl)-4-penten-2-amine and (2R)-(4E)-N-methyl-5-(5-isopropoxy-3-pyridyl)-4-penten-2-amine) are discussed in the Declaration (Table 5). As such, the claim scope is certainly commensurate in scope with the Declaration.

Table 5 of the Declaration demonstrates that both the R and S isomers of N-methyl-5-(5-isopropoxy-3-pyridyl)-4-penten-2-amine have suitable binding affinity, and both overcome the metabolism problem (monoamine oxidase activity at the secondary amine side chain) associated with prior art compounds described in the Caldwell patent that do not include a methyl group alpha to the secondary amine side chain. Although the S compound had a slightly higher binding affinity than the R compound, both compounds have significantly improved properties, with respect to metabolism, than the prior art compounds. Accordingly, the compounds represent non-obvious improvements over the prior art.

With respect to whether the Declaration supports the non-obviousness of the cis(Z) compounds, it is important to note that the Caldwell patent was cited for purposes of obviousness based on the trans(E) compound, (4E)-N-methyl-5-(5-isopropoxy-3-pyridyl)-3-buten-1-amine disclosed in the Caldwell patent. This compound does not include the alpha methyl substitution adjacent to the secondary amine side chain, and therefore, it was reasonable to compare the trans(E) compounds with the alpha methyl substitution, as claimed, with the prior art trans(E)

compounds of the prior art. The Office Action does not provide any reason to suspect that the binding affinity of the claimed Z isomers ((2S)-(4Z)-N-methyl-5-(5-isopropoxy-3-pyridyl)-4-penten-2-amine and (2R)-(4Z)-N-methyl-5-(5-isopropoxy-3-pyridyl)-4-penten-2-amine) would be significantly different than the Z isomer that is not substituted with a methyl group at the alpha position ((4E)-N-methyl-5-(5-isopropoxy-3-pyridyl)-3-buten-1-amine). Further, no sound scientific basis has been presented to question that the Z isomers with the alpha methyl substitution on the secondary amine side-chain would similarly have improved bioavailability (through inhibition of monoamine oxidase activity) relative to the compounds with no alpha methyl substitution. Accordingly, Applicants respectfully assert that the obviousness rejections should be withdrawn.

Provisional Non-statutory Double Patenting Rejections

Claims 21-27 stand provisionally rejected for non-statutory type double patenting over co-pending U.S. applications 08/631,761 and 09/570,226. U.S.S.N. 09/570,226 has issued as U.S. Patent No. 6,455,554. Each claim in the '554 patent is directed toward N-oxide forms of various 3-pyridyl compounds.

The test for obviousness-type double patenting involves examining the claims in the issued patent or co-pending application and determining whether the pending claims would be obvious in view of the claims in the cited patents/patent applications. Applying that test to the instant claims and the claims as issued in U.S. Patent No. 6,455,554, the instantly claimed compounds are not N-oxides, and therefore would not have been obvious in view of the claims of U.S. Patent No. 6,455,554. Accordingly, Applicants respectfully request that the obviousness-type double patenting rejection be withdrawn with respect to U.S. Patent No. 6,455,554. In a telephonic interview with Examiner Balasubramanian held on December 3, 2002, the Examiner indicated that he would withdraw the requirement for a terminal disclaimer in connection with this application/patent.

With respect to co-pending U.S. applications 08/631,761, Applicants herein include a terminal disclaimer. As requested by the Examiner in the December 3, 2002 telephonic interview, the terminal disclaimer also references U.S.S.N. 09/873,419, which is related to the '761 application. The submission of the terminal disclaimer obviates the rejection.

For at least the reasons set forth herein, Applicants submit all of pending claims 21-27 are in condition for allowance. Prompt consideration and action in the form of a Notice of Allowance is thus respectfully requested. Should the Examiner have any questions, he is invited to contact Applicants' undersigned representative at the telephone number below.

Respectfully submitted,

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